Has the sun set on FS in GU system

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Professor, Department of Pathology and Urology Disease Management Group
Tata Memorial Centre, Parel
Purpose of FS in GU

• The purpose of FS diagnosis in the genitourinary tract (GU) is to provide accurate diagnostic information during the intraoperative decision making process to achieve the best patient outcomes.
Clinical benefits of frozen section assessment during urological surgery: Does it contribute to improving surgical margin status and patient outcomes as previously thought?

Hiroshi Miyamoto*

Departments of Pathology and Urology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Abstract: Despite significant advances in patient selection as well as surgical technique over the past few decades, it is still not uncommon for patients with urological malignancy and positive surgical margins to be observed. Meanwhile, intraoperative pathology consultation with frozen section assessment, which generally provides useful information for the optimal procedure, has been widely utilized for the assessment of surgical margins during urological surgeries. Thus, it remains unanswered whether intraoperative frozen section assessment has an impact on final surgical margin status as well as long-term oncological outcomes. The present review summarizes and discusses available data assessing the utility of frozen section assessment of the surgical margins during urological surgeries, such as radical prostatectomy, partial nephrectomy and radical cystectomy. The current findings suggest that select patients might benefit from...
Common indications for frozen section diagnosis in genitourinary surgery
Prostate

- Margin evaluation during radical prostatectomy....rarely sent
- Diagnosis of pelvic lymph node metastasis during radical prostatectomy...occasional
Margins in RP at frozen?

- Rarely sent
- Mostly sent separately by surgeon
- Common- bladder neck tissue, urethral/ apex, preprostatic fat

- Rarely FS diagnosis of a metastatic prostate cancer if there is impending Paraplegia/quadriplegia or impending fracture
Radical prostatectomy - Grossing
studies after 2000 showed that 28.7% of radical prostatectomy specimens with FSA carried out at the neurovascular bundle were positive for a final surgical margin, which was significantly ($P = 0.013$) higher than its rate (13.8%) in the no-FSA cases showing biopsy Gleason score 7 or higher (10.1% vs 15.3%, $P = 0.012$) as well as 8 or higher (16.3% vs 28.6%, $P = 0.048$). Carrying out FSA also resulted in marginal reductions of the margin-positive rate in cases with

<table>
<thead>
<tr>
<th>Study</th>
<th>Specific site</th>
<th>RP with FSA</th>
<th></th>
<th>Final positive SM (%)</th>
<th>RP without FSA</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Goharderakshan et al.</td>
<td>NVB</td>
<td>15/101 (14.9)</td>
<td>12/15 (80.0)</td>
<td>27/101 (26.7)</td>
<td>19/138 (13.8)</td>
<td>0.013</td>
<td></td>
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<tr>
<td>Eichelberg et al.</td>
<td>NVB</td>
<td>35/83 (42.2)</td>
<td>NA</td>
<td>13/83 (15.7)</td>
<td>75/525 (14.3)</td>
<td>0.738</td>
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<tr>
<td>Heinrich et al.</td>
<td>NVB</td>
<td>9/130 (6.9)</td>
<td>NA</td>
<td>1/130 (0.7) at NVB</td>
<td>1/157 (0.6) at NVB</td>
<td>1.000</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>4/130 (3.1) at all sites</td>
<td>9/157 (5.7) at all sites</td>
<td>0.395</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schlammm et al.</td>
<td>NVB</td>
<td>1464/5392 (27.2)</td>
<td>NA</td>
<td>390/2567 (15.2)§</td>
<td>557/2567 (21.7)§</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<tr>
<td>Akin et al.</td>
<td>MRI-directed</td>
<td>28/66 (42.4)</td>
<td>NA</td>
<td>23/66 (34.8)</td>
<td>1/14 (7.1)</td>
<td>0.054</td>
<td></td>
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<tr>
<td>Kakiuchi et al.</td>
<td></td>
<td>60/1128 (5.3)</td>
<td>26/60 (43.3)</td>
<td>109/1128 (9.7)</td>
<td>163/1480 (11.0)</td>
<td>0.264</td>
<td></td>
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<tr>
<td>Petralia et al.</td>
<td></td>
<td>18/134 (13.4)</td>
<td>18/18 (100)</td>
<td>10/134 (7.5)</td>
<td>25/134 (18.7)</td>
<td>0.010</td>
<td></td>
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</tbody>
</table>

†Negative FSA diagnosis was obtained at the initial FSA positive site by additional tissue excision. †Rates of final positive SM between FSA (+) vs FSA (−) cases (re-calculated by the author using the Fisher's exact test). §Propensity score-matched cohort.
Importantly, FSA in these areas has been shown to improve potency rates without compromising surgery. Pathologists receive two types of margin tissues, small fragment(s) of the tumor bed and the entire specimen of a

![Graphs showing recurrence-free survival](image)

**Fig. 1** Recurrence-free survival stratified by (a) cases with vs without FSA, (b) biopsy Gleason score 7 cases with vs without FSA, (c) biopsy Gleason score 4 + 3 = 7 cases with vs without FSA, or (d) all cases with benign vs atypical vs malignant FSA. Comparisons were made by the log-rank test.
Intraoperative Frozen Section of the Prostate Decreases Margin Rate While Ensuring Nerve Sparing Procedure for Radical Prostatectomy

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From the Departments of Urology (CvB, MB, FR, BL, KB, JP, JN, RLP) and Pathology (JBS), Ruhr-University Bochum, and Marienhospital Herne, Herne, Germany, and Department of Epidemiology and Biostatistics, George Washington University, Washington, D.C.

Objectives: To assess the impact of frozen section on bilateral nerve-sparing or selective nerve-sparing prostatectomy and to determine the incidence of false-negative frozen sections.

Methods: This study included 198 patients who underwent radical prostatectomy between 2003 and 2010. Pathologic slides were reviewed to determine the incidence of false-negative frozen sections.

Results: Among the 198 patients, 50 had T3a, 104 had T3b, and 44 had T4 tumors, respectively. The number of patients with any cancer stage was 198. The total number of frozen sections was 22. In 21 cases, the frozen section was positive, leading to immediate prostatectomy. In 1 case, the frozen section was negative, leading to a delay in prostatectomy.

Conclusions: Intraoperative frozen section is a useful tool in bilateral nerve-sparing prostatectomy, allowing for immediate prostatectomy in cases of positive frozen sections and avoiding unnecessary delays in prostatectomy in cases of negative frozen sections.

Keywords: prostatectomy, nerve-sparing, frozen sections, false-negative, prostate cancer.
Intraoperative Nodal assessment in RP

• In patients with high risk disease (Gleason score of 8 and/or high levels of PSA), FS examination of the lymph nodes may be requested since positive lymph nodes by FS may be an important factor in deciding not to perform the RP.

• However, the presence of a microscopic focus of carcinoma is not an absolute contraindication of RP.
Kidney

- Margin evaluation during partial nephrectomy.
- Definitive histological diagnosis of a renal mass.
- Diagnosis of lymph node metastasis

- Rarely FS of a needle core biopsy for urgent diagnosis
Changing presentation of RCC

### TNM-Classification of Renal Cell Carcinoma

<table>
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<tr>
<th></th>
<th>1987</th>
<th>1997</th>
<th>2002</th>
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<tbody>
<tr>
<td>T1</td>
<td>&lt;2.5cm</td>
<td>&lt;7cm</td>
<td>&lt;7cm</td>
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<tr>
<td>T1a</td>
<td>&lt;4cm</td>
<td>&lt;4cm</td>
<td></td>
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<tr>
<td>T1b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>&gt;2.5cm</td>
<td>&gt;7cm</td>
<td>&gt;7cm</td>
</tr>
<tr>
<td>T3a</td>
<td>infiltration perirenal fat, adrenal gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3b</td>
<td>infiltration of renal vein, vena cava</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3c</td>
<td></td>
<td>infiltr. of thoracic v. cava</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td></td>
<td>tumor outside gerota’s fascia</td>
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</table>
Would partial nephrectomy offer a survival advantage over radical nephrectomy.....??
Comparative Effectiveness for Survival and Renal Function of Partial and Radical Nephrectomy for Localized Renal Tumors: A Systematic Review and Meta-Analysis

Simon P. Kim, R. Houston Thompson, Stephen A. Boorjian, Christopher J. Weigt, Leona C. Han, M. Hassan Nased, Nathan D. Shipee, Patricia J. Erwin, Brian A. Costello, George K. Chow, Bradley C. Lebovich

Table 2. Meta-analysis of PN vs RN for ACM, CSM and CKD from generic inverse variance model with random effects

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>ACM</td>
<td>0.81 (0.76–0.87)</td>
<td>0.006</td>
</tr>
<tr>
<td>CSM</td>
<td>0.79 (0.57–1.11)</td>
<td>0.17</td>
</tr>
<tr>
<td>Severe CKD</td>
<td>0.34 (0.20–0.58)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Similar Oncological outcomes

Superior renal functions
DO WE NEED TO SEND THE RESECTED TUMOR FOR FROZEN SECTION ....??

RELAVANCE OF POSITIVE SURGICAL MARGIN
CONCLUSION:
Our population-level data suggest that, although PSMs are fairly prevalent, they appear to have little to no impact on 5-year survival rates.
Margin evaluation of renal NSS

Two types of margins may be sent:

• One is a small piece of tumour bed parenchymal tissue
• The second type of specimen for FS margin evaluation is an entire partial nephrectomy specimen
Nephron sparing surgery: Pathological aspects with emphasis on margins and value of frozen section

Santosh Menon, Ganesh Bakshi★, Gagan Prakash★, Amit Joshi★★, Sangeeta B Desai
Department of Pathology, ★Uro-oncosurgery and ★★Medical Oncology, Tata Memorial Centre, Mumbai
Distribution of malignant renal neoplasms at partial nephrectomy

- 105 cases were malignant:
  - renal cell carcinoma (RCC) - conventional (81),
  - papillary (18),
  - chromophobe (4),
  - mucinous tubular spindle cell carcinoma (1) and
  - Primitive neuroectodermal tumour(1)
Polar distribution
Results

• Majority of the cases (81 cases) had small tumors (pT1a, 56 cases and pT1b, 25 cases; pT=pathologic stage) with
  • Median tumor size = 3.2 cm.
  • Intraoperative frozen consultation margin was positive in 18 /74 cases of which 10 were revised.
  • The margin at frozen section was 1mm - 5mm in 49/74 cases.
  • The mean margin for all cases was 2.1mm.
RESULTS

- Four cases were upgraded to pT3 on final histopathology and 2 of these patients underwent radical nephrectomy.
- Follow-up was available in 62 patients and median follow-up was of 16 months (range 6 - 89 months).
- Two patient of papillary renal cell carcinoma, type 2 had recurrence during follow-up
Positive margin may not adversely affect clinical outcome

• First, surgeons often fulgurate the cortical rim of the NSS bed using .... eradicate any residual cancer cells by virtue of thermal destruction and attain an “additional margin.”

• Second, renal ischemia induced by clamping of the renal artery......eradicate some residual tumor

• Third....low grade tumors....biological course is protracted
<table>
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<tr>
<th>Primary diagnosis of Renal mass/tumor in FS</th>
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<tbody>
<tr>
<td>• Histological diagnosis of renal tumours is seldom needed as it typically does not affect surgical decisions</td>
</tr>
<tr>
<td>• FS diagnosis is requested to distinguish between invasive urothelial carcinoma and high grade renal cell carcinoma (RCC) since their surgery differs.</td>
</tr>
</tbody>
</table>
Urinary bladder pathology

- Surgical margin evaluation during radical or partial cystectomy
- Diagnosis of pelvic peritoneal nodules or masses.
- Diagnosis of pelvic lymph node metastasis during cystectomy
Radical cystectomy - margins

- The incidence of high grade dysplasia/carcinoma in situ (CIS) of the ureteral margins in the published literature ranges from 4.8 to 9%
- Achieving a negative ureteral margin when feasible is desirable for urinary diversion to reduce the risk of recurrence at the ureterointestinal anastomosis.
FS for urothelial tumor during re TURBT

Surgeon question: For tumor grade, invasion and presence/absence of detrusor + or – muscle invasion
Radical cystectomy - Pelvic nodes

- Intraoperative FS diagnosis of the pelvic lymph nodes may be used to determine the extent of nodal dissection,
- But the presence of metastatic disease in the nodes is not an absolute indication for termination of radical procedure.
Testis

• Diagnosis of testicular/ Para testicular lesions for possible testis-sparing operation.
• Diagnosis of lymph node metastasis during retroperitoneal nodal dissection--- almost never done
RESULTS: Twenty-three patients were included in the study. Median follow-up was 10 months (interquartile range: 60). A total of 73.9% of the lesions were benign and 26.1% were malignant. There were no diagnostic changes in relation to the FSE and definitive pathology reports. Diagnostic accuracy measures were 100%. The degree of concordance between the FSE and definitive malignancy reports was statistically significant ($\kappa = 1.0$, $p < 0.05$). As a result of the benign FSE report, 12 radical orchiectomies (70.6%) were prevented. Three patients (12.5%) had grade I complications. In the long term, 2 patients presented with testicular atrophy. No malignant formations were observed during follow-up in the patients that did not undergo radical orchiectomy as a result of the benign FSE report.
CHEVASSU MANEUVER

- Testis-sparing surgery in adults is a safe alternative to radical orchidectomy.
- Small germ cell tumors arising in both or solitary testes
- Non-palpable ultrasound-detected tumors
RP nodes in post chemo NSGCT
RP nodes in post chemo
NSGCT
Penis

- Surgical margin evaluation during partial penectomy
- Diagnosis of inguinal lymph node metastasis. Superficial GND may be converted to complete GND if node positive at FS

- Rarely and dread-ely.....a primary diagnosis during penectomy
FS- Biopsy pathology

Penile intraepithelial neoplasia (PeIN)
Invasive carcinoma
What after a biopsy diagnosis of penile carcinoma???
Summary...Role?? Not much role of FS in GU pathology

- In radical prostatectomy ...mostly no margins, rarely during nerve sparing if surgeon feels
- In nephron sparing surgery....no proven /evidence of sending routine margins. Upper tract urothelial vs RCC...YES to FS
- In radical cystectomy....sending ureter cut margins is questionable ...maybe only if planning RCNB
- In testis....no margins...very rarely 1\(^0\) diagnosis
- In penile....margins if surgeon feels it is close else no need. GND YES to FS
But I hope ...this lecture had a role
Sun will definitely rise and set each day....

Only the next moment will tell you
BUT for FS in GU

• It is mostly a SUNSET.....
Acknowledgements

• Dr Sangeeta Desai
• Dr Ganesh Bakshi
• Dr Gagan Prakash...borrowed some slides from him
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• Dr Mahendra
• Dr Amit Joshi
• Dr Umesh Shetty
• My residents and colleagues- Dr Palgun